federal register

TUESDAY, DECEMBER 6, 1977
PART II

ENVIRONMENTAL PROTECTION AGENCY

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PESTICIDE PROGRAMS

Rebuttable Presumption Against Registration and Continued Registration of Pesticide Products Containing Benomyl

[6560-01]

ENVIRONMENTAL PROTECTION AGENCY

[OPP-30000/23; FRL 822-2]

PESTICIDE PROGRAMS

Rebuttable Presumption Against Registration and Continued Registration of Pesticide Products Containing Benomyl

The Deputy Assistant Administrator, Office of Pesticide Programs, Environmental Protection Agency (EPA), has determined that a rebuttable presumption exists against registration and continued registration of all pesticide products containing benomyl.[1]

I. Regulatory Provisions

A. *General.* Title 40, Part 162.11, of the Code of Federal Regulations for the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended (86 Stat. 973, 89 Stat. 751, 7 U.S.C. 136 *et seq.*), provides that a rebuttable presumption against registration shall arise if the Agency determines that a pesticide meets or exceeds any of the risk criteria relating to acute and chronic toxic effects set forth in § 162.11(a)(3). If it is determined that such a rebuttable presumption has arisen, the regulations require that the registrant be notified by certified mail and afforded an opportunity to submit evidence in rebuttal of the presumption. In addition, the Agency has determined that the public should also be given notice of the bases for the presumption to provide an opportunity for comment and to solicit additional information relevant to the presumption.

A notice of rebuttable presumption against registration is issued when the evidence related to risk meets the criteria set forth in § 162.11(a)(3). It is emphasized that a notice of rebuttable presumption against registration and continued registration of a pesticide is not a notice of intent to cancel the registration of a pesticide, and may or may not lead to cancellation. The notice of intent to cancel is issued only if it is determined that the pesticide may generally cause unreasonable adverse effects to the environment after careful consideration of both the risks and benefits.

Accordingly, all registrants and applicants for registration are invited pursuant to 40 CFR 162.11(a)(4) to submit evidence in rebuttal of the presumptions listed in Part II of this notice. Registrants and other interested parties may also submit for consideration data on benefits registration. In addition, any registrant may petition the Agency to voluntarily cancel a current registration pursuant to Section 6(a)(1) of FIFRA.

B. *Rebuttal Criteria.* Section 162.11(a)(4) provides that a registrant may rebut the presumption by sustaining the burden of proving:

(1) In the case of a pesticide presumed against pursuant to the acute toxicity or lack of emergency treatment criteria, "that when considered with the formulation, packaging, method of use, and proposed restrictions on and directions for use and widespread and commonly recognized practices of use, the anticipated exposure to an applicator or user and to local, regional, or national populations of nontarget organisms is not likely to result in any signficant acute adverse effects" (40 CFR 162.11(a)(4)(i));

(2) In the case of a pesticide presumed against pursuant to the chronic toxicity criteria, "that when considered with proposed restrictions on use and widespread and commonly recognized practices of use, the pesticide will not concentrate, persist or accrue to levels in man or the environment likely to result in any significant chronic adverse effects" (40 CFR 162.11(a)(4)(ii)); or

(3) In either case, that "the determination by the Agency that the pesticide meets or exceeds any of the criteria for risk was in error" (40 CFR 162.11(a)(4)(iii)).

C. *Benefits Information.* In addition to submitting evidence to rebut the presumption of risk, Section 162.11(a)(5)(iii) provides that a registrant "may submit evidence as to whether the economic, social and environmental benefits of the use of the pesticide subject to the presumption outweigh the risk of use." If the risk presumptions are not rebuted, the benefit evidence submitted by the registrant,[2] applicants, and other interested persons will be considered by the Administrator in determining the appropriate regulatory action. Specifically, § 162.11(a)(5)(iii) provides that if the "benefits appear to outweigh the risks," the Administrator may issue a notice of intent to hold a hearing pursuant to Section 6(b)(2) of FIFRA rather than a notice of intent to cancel or deny registration pursuant to Section 3(c)(6) of FIFRA. Alternatively, if the "benefits do not appear to outweigh the risks, the Administrator shall issue a notice pursuant to Section 3(c)(6) or Section 6(b)(1) of the Act, as appropriate." Moreover, if at any time the Administrator determines that a pesticide poses an "imminent hazard" to humans or the environment, a notice of suspension may be issued pursuant to Section 6(c) of the Act.

Stated below are the § 162.11(a)(3) risk criteria which the Agency has found to have been met or exceeded by registrations and applications for registration of pesticide products containing benomyl. The Agency's basis for concluding that these risk criteria have been met or exceeded is set out in "Benomyl: Position Document 1," which follows. Copies of attachments to the Position Document which are not published with this notice are available for public inspection in the Office of Special Pesticide Reviews. Information protected from disclosure pursuant to FIFRA Section 10 cannot be provided. Specific inquiries concerning the Position Document, as well as requests for access to these files, should be directed to Project Manager Mrs. Esther Saito, Office of Special Pesticide Reviews (WH-566), EPA, room 447, East Tower, 401 M St. SW., Washington, D.C. 20460, 202-755-8050.

II. Presumptions

A. *Acute Toxicity: Hazard to Wildlife, Aquatic Species.* 40 CFR Section 162.11(a)(3)(i)(B)(3) provides that a rebuttable presumption shall arise if a pesticide "(r)esults in a maximum calculated concentration following direct application to a 6-inch layer of water more than ½ the acute LC_{50} for aquatic organisms representative of the organisms likely to be exposed as measured on test animals specified in the Registration Guidelines."

On the basis of scientific studies and information summarized in the Position Document, the Agency has concluded that this risk index has been exceeded by all registrations and applications for registration of pesticide products containing benomyl which are for direct application to water, and that a rebuttable presumption against new or continued registration of such products has therefore arisen.

B. *Mutagenicity.* 40 CFR § 162.11(a)(3)(ii)(A) provides that a rebuttable presumption shall arise if a pesticide "* * * induces mutagenic effects, as determined by multitest evidence."

On the basis of scientific studies and information summarized in the Position Document, the Agency has concluded that this risk index has been exceeded by all registrations and applications for registration of pesticide products containing benomyl, and that a rebuttable presumption against new or continued registration of such products has therefore arisen.

[1] A position document containing an appendix of references, background information, and other material pertinent to the issuance of this notice, has been prepared by the Agency Working Group on benomyl and is also published with this notice.

[2] Registrants or other interested persons who desire to submit benefit information should consider submitting information on the following subjects, along with any other relevant information they desire to submit:

1. Identification of the major uses of the pesticide, including estimated quantities used by crop or other application.

2. Identification of the minor uses of the pesticide, including estimated quantities used by category such as lawn and garden uses and household uses.

3. Identification of registered alternative products for the uses set forth in (1) and (2) above, including an estimate of their availability.

4. Determination of the change in costs to the user of providing equivalent pesticide treatment with any available substitute products.

5. Assessment of regulation impact upon user productivity (e.g., yield per acre and/or total output) from using aavilable substitute pesticides or from using no other pesticides.

6. If the impacts upon either user costs or productivity are significant, a qualitative assessment of the regulation's impact on production of major agricultural commodities and retail food prices of such commodities.

C. *Other Chronic or Delayed Toxic Effects.* 40 CFR § 162.11(a)(3)(ii)(B) provides that a rebuttable presumption shall arise if a pesticide "[p]roduces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety * * *."

On the basis of scientific studies and information summarized in the Position Document, the Agency has concluded that the risk index for teratogenicity has been exceeded by all registrations and applications for registration of pesticide products containing benomyl which are for home use, and that a rebuttable presumption against new or continued registration of such products has therefore arisen.

On the basis of scientific studies and information summarized in the Position Document, the Agency has concluded that the risk index for reduction in spermatogenic activity has been exceeded by all registrations and applications for registration of pesticide products containing benomyl and that a rebuttable presumption against new or continued registration of such products has therefore arisen.

D. *Population Reductions in Nontarget Organisms.* 40 CFR § 162.11(a)(3)(ii)(C) provides that a rebuttable presumption shall arise if a pesticide "[c]an reasonably be anticipated to result in significant local, regional, or national population reductions in nontarget organisms * * *"

On the basis of scientific studies and information summarized in the Position Document, the Agency has concluded that the risk index for population reductions in nontarget organisms has been exceeded by registrations and applications for registration of pesticide products containing benomyl which are for outdoor use, and that a rebuttable presumption against new or continued registration of such products has therefore arisen.

III. Additional Grounds For Review

As discussed in more detail in the attached Position Document, benomyl has the potential of reacting with nitrites to form N-nitroso compounds. Some N-nitroso compounds are known to possess oncogenic properties. The data and analysis available at this time with respect to the potential formation of oncogenic compounds are not sufficient to warrant the issuance of a Rebuttable Presumption. The Agency specifically solicits further evidence bearing on the likelihood and significance of such reaction. All comments and information received with respect to this potential reaction, including analysis thereof, may serve as a basis for a final decision as to the registrability of benomyl pesticides [40 CFR 162.11(a)(6)].

IV. Registrations and Products Subject to the Notice

All registrants and applicants for registration listed below are being notified by certified mail of the rebuttable presumption existing against registration and continued registration of their products.

The registrants and applicants for registration shall have 45 days from the date this notice is sent or until January 23, 1978 to submit evidence in rebuttal of the presumption. However, the Administrator may, for good cause shown, grant an additional 60 days during which such evidence may be submitted. Notice of such an extension, if granted, will appear in the Federal Register.

A registrant or applicant for registration may, if it desires, assert a business confidentiality claim covering part or all of the information submitted in rebuttal. The registrant or applicant may assert the claim by placing on or attaching to the information a cover sheet, stamped or typed legend, or other suitable form of notice employing language such as "trade secret," "proprietary," or "company confidential." Allegedly confidential portions of otherwise nonconfidential documents should be clearly marked.

If a confidentiality claim is asserted, the information covered by the claim will be disclosed by EPA only to the extent and by means of the procedures set forth in 40 CFR 2, Subpart B (41 FR 36906, September 1, 1976). If no confidentiality claim accompanies the information at the time it is received by EPA, EPA will place the information in the public comment file where it will be available for public inspection.

If a registrant or applicant does assert a confidentiality claim for some, but not all, of the information submitted to EPA in rebuttal, the registrant or applicant should furnish two copies of the information to EPA. The first copy should contain all of the information submitted in rebuttal with information claimed as confidential clearly identified. The second copy should be identical to the first except that all information claimed as confidential should be deleted. The second copy will be placed in the public comment file. The first copy will be treated in accordance with the procedures set out above.

V. Duty To Submit Information on Adverse Effects

Registrants are required by law to submit to EPA any additional information regarding any adverse effects on man or the environment which comes to a registrant's attention at any time, pursuant to Section 6(a)(2) of FIFRA and 40 CFR 162.8(d). If any registrant of benomyl product has any published or unpublished information, studies, reports, analyses, or reanalyses regarding any adverse effects in animal species or humans, residues, and claimed or verified accidents to humans, domestic animals, or wildlife, which *have not* been previously submitted to EPA, the material must be submitted immediately. When responding to this notice, each registrant shall submit a written certification to the Agency that all information regarding any adverse effects known to the registrant has been submitted. In addition, the registrants should notify EPA of any studies currently in progress, including the purpose of the study, the protocol, the approximate completion date, and a summary of all results observed to date.

VI. Public Comments

During the time allowed for submission of rebuttal evidence, specific comments on the presumptions set forth in this notice and on the material contained in the Position Document are solicited from the public. In particular, any documented episodes of adverse effects to humans, domestic animals, or wildlife, and information as to any laboratory studies in progress or completed, are requested to be submitted to EPA as soon as possible. Specifically, information on the fate and effects of Benomyl, its impurities, metabolites, and degradation products on flora and fauna, particularly animals with metabolism similar to that in humans, is solicited. Similarly, any studies or comments on the benefits from the use of Benomyl are requested to be submitted. All comments and information received, as well as any other relevant information and analysis thereof, which come to the attention of the Agency may serve as a basis for final determination pursuant to § 162.11(a)(5).

All comments and information should be sent to:

Federal Register Section, Technical Services Division (WH-569), Room 401 East Tower, 401 M Street SW., Washington, D.C. 20460.

Three copies of the comments or information should be submitted to facilitate the work of the Agency and others interested in inspecting them. The comments and information should bear the identifying notation "OPP-*30000/23*." Comments and information received within the specified time limit shall be considered before it is determined whether a notice shall be issued in accordance with 40 CFR 162.11(a)(5)(ii).

Comments received after the specified time period will be considered only to the extent feasible, consistent with the time limits imposed by 40 CFR 162.11(a)(5)(ii). All written comments and information filed pursuant to this notice will be available for public inspection in the office of the Federal Register Section from 8:30 a.m. to 4 p.m. during normal working days.

Interested persons are encouraged to take advantage of the opportunity to inspect Agency files during normal working hourse since (1) all of the information received may serve as a basis for final determination pursuant to 162.11(a)(5) and (2) the Agency will not generally publish a summary of information received in the Federal Register at the the close of the rebuttal period.

Your cooperation is solicited in identifying any errors or omissions which may have been made in the following computer listings. Corrections to the listings may not necessarily be published in

the FEDERAL REGISTER, but rather handled by mail with affected parties. Omissions will be corrected by notice in the FEDERAL REGISTER.

Dated: November 23, 1977.

EDWIN L. JOHNSON,
Deputy Assistant Administrator for Pesticide Programs.

BENOMYL: POSITION DOCUMENT 1

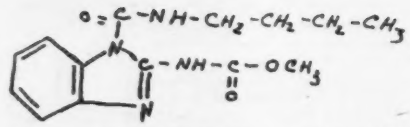
BENOMYL WORKING GROUP, ESTHER SAITO, PROJECT MANAGER, OFFICE OF SPECIAL PESTICIDE REVIEWS, U.S. ENVIRONMENTAL PROTECTION AGENCY

I. BACKGROUND

A. CHEMISTRY

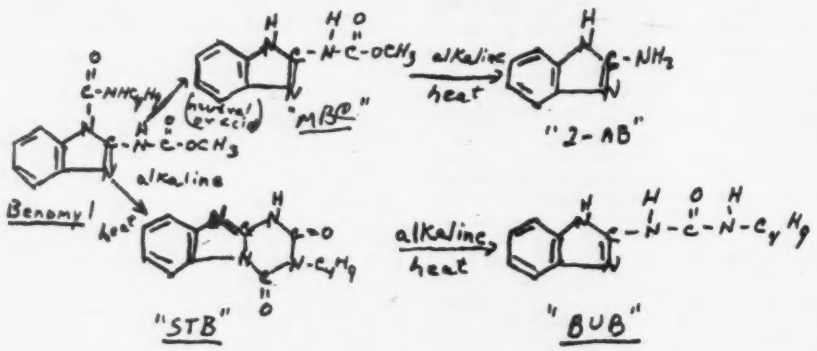
1. *General Chemistry.* Benomyl is the common name for the chemical methyl 1-(butylcarbamoyl)-2-benzimidazolecarbamate. First introduced in 1967 as an experimental fungicide under the code name "DuPont 1991," benomyl is also sold under the trade names Benlate® and Tersan® 1991.

Benomyl has the molecular formula $C_{14}H_{18}N_4O_3$ and a molecular weight of 290. The structural formula is:



Benomyl is made by the reaction of the condensation product of o-phenylene diamine and $NCNHCOOCH_3$ with n-butyl isocyanate (1). Benomyl, a white crystalline solid with a faint acrid odor, decomposes before melting. It is essentially insoluble in water or oils, but it is soluble in acetone, chloroform, and xylene. It is not volatile at room temperature or corrosive to metals.

Figure 2 outlines the chemical breakdown of benomyl under laboratory conditions (2). In aqueous solution benomyl is hydrolyzed to methyl 2-benzimidazole carbonate (MBC) and butyl isocyanate. Under alkaline conditions MBC hydrolyzes to 2-aminobenzimidazole (2-AB). Direct alkaline treatment of benomyl yields 3-butyl-S-triazino [1.2a] benzimidazole-2.4(1H,3H) dione (STB), which is unstable in hot alkali and is converted to 2-(3-butylureido)-benzimidazole (BUB).



It does not appear that the metabolites formed upon direct alkaline treatment under laboratory conditions are formed in nature. Baude and co-workers were unable to find residues of BUB and STB in leaves sprayed with benomyl; MBC residues were present (3). Data from studies on rats, dogs, dairy cows, and chickens indicate that benomyl is metabolized to methyl 5-hydroxy-2-benzimidazolecarbamate (5-HBC) and its isomer methyl 4-hydroxy-2-benzimidazolecarbamate (4-HBC) (4).

2. *Residue Chemistry.*—(a) *Soil.* The half-life for all benzimidazole-containing residues of benomyl (calculated as benomyl and hereafter referred to as BIA metabolites) is approximately 3 to 6 months on turf and about 6 to 12 months on bare soil; the major portion of the residues is found in the top 4 inches of soil (5). Using ^{14}C-labeled material, Rhodes and co-workers found that benomyl and the metabolites MBC and 2-AB are essentially immobile in soil and do not leach or move significantly from the site of application (6).

In 1973 the Technical Services Division (TSD) of the Office of Pesticide Programs (OPP) of the Environmental Protection Agency monitored farms in Oregon, Washington, and New York where benomyl had been applied. Benomyl was found in 64 percent of the 45 soil samples analyzed by the Ecological Monitoring Branch of TSD. Residue concentrations ranged from undetectable amounts to 4.58 parts per million (ppm), with an arithmetic mean of 0.48 ppm (7).

(b) *Animals.* Benomyl is normally metabolized in animals to 5-HBC, which apears in the urine as glucuronide and/or sulfate conjugates. Other possible degradation products in animal systems include MBC and 4-HBC. Metabolic studies (4, 8) indicate that benomyl and its metabolites do not accumulate in animal tissues but are eliminated rather rapidly as sulphate or glucuronide conjugates in the urine or feces.

No benomyl-MBC residues were detected in milk from dairy cows fed benomyl (up to 50 ppm) when the minimum level of detection was 0.02 ppm. No residues of 5-HBC or 4-HBC were detected in milk of cows fed 2 ppm benomyl in the diet when the minimum level of detection was 0.01 ppm. At this level of sensitivity only 5-HBC was detectable when the animals were fed 10 ppm. In cows fed 50 ppm the average combined residue of 5-HBC and 4-HBC in the milk was about 0.1 ppm (4).

No residues of benomyl or any of its metabolites were detected (level of sensitivity 0.02 ppm) in eggs from chickens fed 5 ppm benomyl in their diet, and only 5-HBC (0.03 to 0.06 ppm) was found in eggs from chickens fed 25 ppm benomyl (4).

(c) *Plants.* Studies of the systemic uptake of benomyl after foliar treatments indicate that relatively small amounts of residues can penetrate the leaf surface and translocate to untreated portions of the plant. Although more benomyl than MBC penetrates and moves through the leaf cuticle, systemic translocation involves primarily MBC and to a lesser degree 2-AB (9, 10). The translocated residues are carried by the intercellular transpiration stream toward the edges and tips of leaves, where they then accumulate. Benomyl is readily absorbed through the root-system of plants (11).

Benomyl remains on foliar surfaces as a relatively stable residue, only gradually degarding to MBC. In one study benomyl residues on the leaves of apple, cucumber, banana, orange, and grape plants 21 to 23 days after treatment were estimated at 48 to 77 percent of the combined residues of benomyl and MBC (3).

In oranges stored for 2 months after post-harvest dipping the amount of residual ^{14}C-benomyl (benomyl and MBC) decreased slowly. Only a small amount was found in the flesh, where as the major portion remained in the peel. Two weeks after application, 61 percent of the surface residues remained unchanged; 38 percent had been converted to MBC (12).

(d) *Water.* On contact with water benomyl rapidly breaks down to MBC, conversion being complete within a week (13).

B. *Registered Uses and Production.* Dupont is the only registered producer of technical grade benomyl in the United States. Under Sections 7(c) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) manufacturers and formulators are required to submit information on production, sales, and distribution. Under Section 10, this information is considered confidential and cannot be released to the public, but it is made available to the Administrator in a confidential appendix to this report (14).

There are 27 products Federally registered by 18 registrants. Fourteen State registrants have applied under 40 CFR 162.17 for Federal registration of 49 products. Eight products not previously registered have been submitted by four applicants.

Of the 27 Federally registered benomyl

formulations 19 are 50 percent wettable powders; 4 are 1.1 to 1.6 percent granular formulations, 2 are 3 and 10 percent solutions registered for postharvest dipping against fruit rot, and 1 is 1.95 percent benomyl in fertilizer for use on turf.

Benomyl is registered for use as a fungicide on fruits, nuts, and vegetables before and after harvest; on rice to control blast and stem rot; on bulbs, corms, and ornamental crops to control basal rot; on elm trees to control Dutch elm disease; and as a fungicide on flowers, ornamentals, shade trees, grasses, and roses.

II. Regulatory History

The first registration for a product containing benomyl was granted July 1, 1970, to duPont (EPA Registration Number 352-354). Tolerances (40 CFR 180.294) have been established for residues of benomyl and its BIA metabolites in or on raw agricultural commodities.

TABLE 1.—*Benomyl Tolerances*

Commodities:	Tolerance (ppm)
Almond hulls	1
Avocados	1
Apples (pre- and postharvest)	7
Apricots (pre- and postharvest)	15
Bananas (pre- and postharvest)	1
Banana pulp	.2
Beans	2
Bean vine (forage)	50
Blackberries	7
Blueberries	7
Boysenberries	7
Cattle (fat)	.1
Cattle (meat byproduct)	.1
Cattle (meat)	.1
Celery	3
Cherries (pre- and postharvest)	15
Citrus fruits (pre- and postharvest)	10
Cucumbers	1
Dewberries	7
Eggs	.1
Goats (fat)	.1
Goats (meat byproduct)	.1
Goats (meat)	.1
Grapes	10
Hogs (fat)	.1
Hogs (meat byproduct)	.1
Hogs (meat)	.1
Horses (fat)	.1
Horses (meat byproduct)	.1
Horses (meat)	.1
Loganberries	7
Mangoes	3
Melons	1
Milk	.1
Mushrooms	10
Nectarines (pre- and postharvest)	15
Nuts	.2
Peaches (pre- and postharvest)	15
Peanuts	.2
Peanut forage	15
Peanut hay	15
Peanut hulls	2
Pears (pre- and postharvest)	7
Pineapples (postharvest)	35
Plums (pre- and postharvest, including fresh prunes)	15
Poultry (fat)	.1
Poultry (liver)	.2
Poultry (meat byproduct)	.1
Poultry (meat)	.1
Pumpkins	1
Raspberries	7
Rice	5
Rice straw	15
Sheep (fat)	.1
Sheep (meat byproduct)	.1
Sheep (meat)	.1
Soybeans	.2
Squash (summer and winter)	1
Strawberries	5
Sugar beet roots	.2
Sugar beet tops	15
Tomatoes	5

The tolerance for the combined residues of benomyl and its BIA metabolites in raisins is 50 ppm, when the residue is present as a result of application of the fungicide to growing grapes (21 CFR 193.30).

The following tolerances for benomyl as a food additive have also been established (21 CFR 561.50):

"125 parts per million in dried grape pomace and raisin waste when present therein as result of application of the fungicide to growing grapes.

70 parts per million in dried apple pomace when present therein as a result of application (preharvest and/or postharvest) of the fungicide to the raw agricultural commodity apples.

50 parts per million in dried citrus pulp when present therein as a result of application (preharvest and/or postharvest) of the fungicide to the raw agricultural commodity citrus fruits.

20 parts per million in or on rice hulls when present therein as a result of preharvest application of the fungicide to the raw agricultural commodity rice."

III. Summary of Scientific Evidence to Support Rebuttable Presumption

40 CFR 162.11(a)(3) provides that a rebuttable presumption shall arise if a pesticide's ingredients, metabolites, or degradation products meet or exceed (i) acute toxicity risk criteria relating to hazards to humans, domestic animals, or wildlife, or (ii) chronic toxicity risk criteria relating to humans and to population reductions in nontarget organisms or fatality to members of endangered species.

A. Acute Toxicity: Hazard to Aquatic Organisms

Section 162.11(a)(3)(i)(B)(3) specifies that a rebuttable presumption shall arise against a pesticide if its direct application to a 6-inch layer of water according to label instructions results in concentrations greater than one-half the acute LC_{50} for aquatic organisms likely to be exposed.

It can be calculated that application of pesticide products containing benomyl labeled for use against rice blast and stem rot at a rate of up to 2 pounds/acre results in a concentration of 734 ppb (0.734 ppm) in a 6-inch layer of water (15), an amount that is greater than one-half the acute LC_{50} for bluegill sunfish, channel catfish, and *Daphnia magna* (Table 2).

TABLE 2.—*The 96-hr LC_{50} for Bluegill Sun and Channel Catfish and the 48-hr LC_{50} for Daphnia magna*

Organism	LC_{50}	Appendix
Bluegill sunfish	1.2 p/m	16
Do	26 p/m	17
Do	0.2 p/m	18
Do	0.4-0.5 p/m	18
Channel catfish:		
Yolk sac	8-10 p/b	19
6-day-old fry	12 p/b	19
12-day-old fry	10 p/b	19
Daphnia magna	0.64 p/m [1]	20

[1] 48-hr LC_{50} value.

Differences in the temperature of the water in which the fish were kept or in the fish's weights could account for the differences in LC_{50} figures for bluegill sunfish (15).

Because the calculated residue of benomyl (734 ppb) in water after its direct application according to label directions is greater than one-half the acute LC_{50} for bluegill sunfish, channel catfish, and *Daphnia magna* the criterion of Section 162.11(a)(3)(i)(B)(3) is exceeded. Accordingly, the Working Group concludes that a presumption has arisen against pesticide products containing benomyl which are registered for direct application to water.

B. Chronic Toxicity

1. *Mutagenic Effects in Multitest Systems.* 40 CFR 162.11(a)(3)(ii)(A) provides that a rebuttable presumption shall arise if a pesticide's ingredients, metabolites, or degradation products induce mutagenic effects, as determined by multitest evidence.

Benomyl and its metabolite MBC have been shown to effect somatic chromosomal abnoramlities and point (gene) mutations in microbial and mammalian test systems. Further evidence of the mutagenic effects of these compopnds has been obtained in studies of plants. Benomyl and MBC have also been shown to reach gonadal tissues in mammals with physiological effects; hence it has the potential of interacting with the genetic material of gametes.

(a) *Chromosomal Effects.*—(i) *Mammalian Cells in Culture.* Benomyl and MBC have been shown to cause mitotic delay (21), a low incidence of chromosomal breakage (21), and multi-nucleation (21, 22) in human, mouse, and hamster cell lines.

(ii) *Mammalian Tests in Vivo.* Metaphase arrest and micronuclei formation occurred in bone marrow cells of rats treated with MBC; in addition there was a low frequency of chromosomal breakage and formation of anaphase bridges. Benomyl caused similar abnormal arrangements when given by intraperitoneal injection but not orally (21).

Seiler (1976) found that benomyl and MBC both produced dose-related mutagenic effects in the micronucleus test in mice. In addition, lagging chromosomes, anaphase bridges, unequally distributed

chromosomes, and tripolar anaphases appeared in mitotic bone marrow cells of treated animals; none of these effects was noted in control cells (23). The author concluded that the main action of benomyl was the inhibition of the mitotic spindle, which may predispose to nondisjunctional errors. The finding of anaphase bridges indicates that benomyl can break chromosomes.

Benomyl administered in doses up to 0.25% of the diet did not increase the frequency of dominant lethal mutations in the rat (24).

(iii) *Plants.*

Higher Plants

The incidence of chromosomal abnormalities, including breaks and exchanges, increased in barley and broad beans treated with benomyl (25). On the other hand, no clear-cut chromosomal mutagenic effect was found in treated onion root-tip cells and yye pollen mother cells (26,27). In another study of onion root-tip cells the increase in the frequency of chromosomal aberrations, which were apparently anaphase bridges and mitotic nondisjunctions, was slight but significant (28).

Lower Plants

Benomyl interfered with normal nuclear division in *Saccharomyces ceresiae* and *Ustilago maydis* (10) and in *Botrytis cineara* (28); MBC had a similar effect in *Aspergillus nidulans* (29). Interference with cell division may predispose to chromosomal nondisjuction.

(b) *Point Mutations.*—(i) *Plants.* When conidia of *Fusarium oxysporum* were treated with benomyl, auxotrophic mutants were isolated at rates significantly greater than the conrtol rate (27).

(ii) *Bacteria.* Two studies have reported that MBC, benomyl, and other benzimidazoles induce base-substitution mutations as detached by the Ames test without metabolic activation. *Salmonella typhimurium* strains *his* G46, TA1530, and TA1535 were used in the tests. Forward mutations were induced in *Salmonella* strain LT-2 by MBC; reverse mutations were induced in *Escherichia coli* strain WP2 uvrA but not in strain WP2, which is excision proficient (30, 31). Mutations appear to result from the incorporation of benzimidazoles into DNA in place of purine bases (32); it has been hypothesized that mutation occurs when the abnormal base is recognized by the cell but the defect is not repaired correctly (31). One study indicates that benomyl does not produce mutations in *Salmonella typhimurium* without activation or in the rodent host-mediated assay (33).

(c) *Other Studies Bearing upon Mutagenicity.* Benomyl, MBC, and some other benzimidazole fungicides induced genetic segregation in a diploid strain of *Aspergillus nidulans* which was heterozygous for spore-color markers and nutritional mutants (34).

The fact that repeated oral doses of MBC, and to a minimal extent benomyl, produced toxic effects in rat testes shows that these compounds can affect the primary reproductive tissues (21).

Since some decrease in spermatogenic activity in dogs and rats was reported to have been caused by acute inhalation exposure (35, 36), it can be concluded that benomyl reaches the gonads. The fact that degeneration of testicular tissue has been demonstrated in Sprague-Dawley rats fed high amounts of MBC (37) indicates that MBC is also transported to the gonads.

The Working Group concludes from these studies that benomyl and MBC are mutagenic in multitest systems. Accordingly, a rebuttable presumption has arisen against all pesticide products containing benomyl.

2. *Adverse Reproduction Effects of Benomyl.* 40 CFR 162.11(a)(3)(ii)(B) provides that a rebuttable presumption shall arise if a pesticide produces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, when ample margins of safety are taken into account.

Benomyl has been shown to induce teratogenic effects in Wistar rats and cause a reduction in spermatogenic activity in both rats and dogs.

Unlike presumptions based on the risk criteria for oncogenicity and mutagenicity, the EPA regulations require that presumptions based on "other chronic effects" criteria, such as teratogenicity and other reproductive effects, must take into account human exposure in determining whether the criteria have been exceeded. The Working Group is unaware of any definitive data indicating the precise quantities of benomyl to which humans are exposed. The Working Group has, therefore, relied on assumptions to determine levels of benomyl to which humans might be exposed.

The Working Group recognizes that its calculations are based on theoretical assumptions rather than on empirical evidence, none of which is available. The Working Group recommends that the Agency solicit further data on exposure from actual use.

(a) *Teratogenic Effects.* The Working Group has considered three papers on teratogenic effects, which have been reviewed by Battelle Memorial Laboratories (38). Schtenberg and Torchinski orally administered benomyl in doses up to 125 mg/kg/day in vegetable oil to Wistar rats either from day 1 to 20 or from day 7 to 15 of gestation. Teratogenic effects including brain hernias, hydrocephalia, microphatalmia and anophthalmia were observed (39). The no-observable-effect level in this study was 62.5 mg/kg/day. Torchinski induced teratogenic effects in Wistar rats by administering benomyl (145 mg/kg) by gavage on day 12 of gestation (40).

The third paper (24) which includes a study of the teratogenic effects of benomyl, suggests that a diet containing 0.50 percent benomyl (calculated by Battelle to be about 400 mg/kg/day) was not teratogenic to Charles River-CD rats. It is difficult to draw definitive conclusions from the results of this study because the actual dose of chemical ingested by the rats was not accurately measured.

Although benomyl is used extensively on food crops, Food and Drug Administration has not monitored benomyl residues in food in its Market Basket Survey (41). The Working Group has, therefore, estimated the possible levels of exposure to benomyl on food by assuming that benomyl would be present in foods in amounts established by tolerances. The Working Group further assumed that the percentages of foods in the total diet would be those calculated by Lehman (42). The Working Group has made these assumptions for lack of empirical data, but, in the absence of actual residue data, we feel these estimates are the best available.

If benomyl is present on foods in amounts established by tolerances and if the food factors of Lehman are used (42), the estimated total daily intake of benomyl calculated for a 60-kg adult who eats 1.5 kg of food per day is approximately 1.8 mg/day or 0.03 mg/kg per day (43). Although the evidence indicates benomyl is teratogenic in Wistar rats and may not be teratogenic in Charles River-CD, the Working Group has used the no-observable-effect level in the more sensitive strain in order to determine margins of safety. The no-observable-effect level found in the Schtenberg and Torchinski study is sufficiently greater than the anticipated exposure from food intake alone for the Working Group to conclude that current uses of benomyl on food crops would pose no unreasonable teratogenic risk to humans (44).

Human exposure from home use products is more difficult to determine. The Working Group is unaware of any studies which provide empirical data on exposure from home use. It is probable that a women of child-bearing age would be exposed to benomyl from home garden use in addition to residues present in foods. In estimating the probable exposure the Working Group has used a benomyl concentration of 600 ppm, the highest used in home sprays prepared according to label directions.

The Working Group assumed that a person could come in contact with as much as a pint of liquid during spraying (45). Although no data on dermal absorption of benomyl were available to the Working Group, it was assumed that no more than 10% would be absorbed.

Using these assumptions, the Working Group calculated a theoretical dermal exposure of approximately 28.5 mg of benomyl per application, or 0.48 mg/kg for a 60-kg woman (46). A person might be exposed to additional, unquantifiable amounts of benomyl through inhalation or accidental ingestion of benomyl from contaminated hands. The theoretical amount of benomyl absorbed during

home garden use would be more than 10 times that from ingestion of treated foods.

On the basis of its calculations, the Working Group concludes that the amount of benomyl to which women of child-bearing age might be exposed is too high relative to the dose which has produced teratogenic efforts in animals. Accordingly, a rebuttable presumption has arisen pursuant to § 162.11(a)(3)(ii)(B) against pesticides containing benomyl which are registered for home use.

(b) *Reduction in Spermatogenic Activity.* Acute and subacute oral studies identify the testes as a primary target of benomyl. Testicular damage occurred with degeneration of germinal tissue and resultant aspermatogenesis at dosage levels of 3400 mg/kg and higher (47). Reduction of sperm was noted both in rats administered a single dose (670 mg/kg) (48) and 10 doses (200 mg/kg/dose) (47). In two chronic feeding studies of dogs and rats, however, the administration of up to 2500 ppm of benomyl the in diet did not demonstrate an effect on sperm production (49). A three-generation reproduction study shows no effect in the fertility index of rates fed up to 2500 ppm of benomyl in their diet (24).

In view of this, the Working Group has concluded that current uses of benomyl on food crops would pose no unreasonable risk of reduction in spermatogenic activity.

In addition to human exposure to benomyl from food intake, the Working Group considered the risk to applicators. The Working Group is unaware of any studies which provide empirical data on applicator exposure, but it is clear that the applicator might be exposed to benomyl through inhalation, oral, and/or dermal contact.

Although the Working Group only considered inhalation exposure in evaluating this risk, it is aware that oral or dermal exposure might also occur. Inhalation toxicity studies show a reduction in spermatogenic activity in rats and dogs exposed to benomyl at dose levels of 33 mg/kg and 82 mg/kg, respectively. In these studies no effects were observed at dose levels of 7.5 mg/kg in rats or 32 mg/kg in dogs (36, 50). The Working Group has used the no-observable-effect level (7.5 mg/kg) in the more sensitive species in order to evaluate the margins of safety.

Based on the author's calculations, the amount of benomyl which an applicator would inhale during 4 hours of spraying is 0.24 mg/kg (51).

On the basis of these calculations, the Working Group concludes that the amount of benomyl to which applicators might be exposed is too high relative to the dose which has produced a decrease in spermatogenic activity in animals. Accordingly, a rebuttable presumption against all pesticides containing benomyl has arisen pursuant to § 162.11(a)(3)(ii)(B).

3. *Effects on Nontarget Organisms: Reduction in Populations of Earthworms.* 40 CFR 162.11(a)(3)(ii)(C) provides that a rebuttable presumption shall arise if a pesticide's ingredients, metabolites, or degradation products can reasonably be anticipated to result in significant local, regional, or national population reductions in nontarget organisms.

The Agency staff has evaluated the methodology, protocol, and conclusions of each of several studies that indicate that benomyl is highly toxic to earthworms. In studies by Stringer and Wright (52) earthworm populations were "virtually eliminated" in apple orchard plots sprayed with benomyl. In addition, benomyl was repellent to earthworms, apparently because it made food materials unpalatable to them. The spraying of benomyl in orchards reduced not only the number and biomass of all earthworm species combined, but also that of each individual species (53). In experiments by Tomlin and Gore (54) application of benomyl to pastures reduced earthworm populations by over 90 percent. Black and Neely (55) found that soil injection at a rate of 36 g/m^2 reduced the earthworm population by 80 percent.

The literature suggests that treatment with benomyl does not permanently reduce most earthworm populations and that they will return to normal within 2 years after treatment is discontinued (55). However, Stringer and Lyons found that populations of two species of earthworms had not returned to normal even after benomyl application had been discontinued for 2 years (53). Since most uses of benomyl require its application at least several times a year, long-term effects, such as changes in species diversity, might well occur in areas of intensive benomyl use.

Tomlin and Gore (54) noted that the earthworm's ability to break down leaf litter, aerate the soil, and distribute nutrients makes it an important factor in establishing soil fertility, especially in noncultivated soils. Stringer and Lyons stated that earthworms are generally regarded as beneficial animals in maintaining soil fertility, but noted that it has not been rigorously proven that they are essential (53). Because it is not clear how earthworms affect soil ecology, the importance of maintaining viable populations of earthworms is open to question. Thus, the Working Group is unable to adequately evaluate the environmental, agricultural, and economic significance of these population reductions. Comment is, therefore, especially solicited on the relevance, impact, and long-term significance of such local population reductions.

The Working Group recognizes that many other factors contribute to the size of earthworm populations, including soil composition, moisture, temperature, cultivation practices, and the use of other pesticides. Furthermore, it appears that the adverse effects on earthworms are generally limited to areas of application and do not extend significantly to adjacent areas. That is, the effects appear to be confined largely to privately owned land, the owners of which can be made aware of the likely effects on earthworms. Nonetheless, it is clear that the use of benomyl according to current label directions can reasonably be expected to result in significant local reductions of earthworm populations. Accordingly, the Working Group concludes that a rebuttable presumption has arisen against pesticide productions containing benomyl which are registered for outdoor use.

IV. Other Adverse Effects: Potential Formation of N-Nitroso Compounds

40 CFR 162.11(a)(3)(ii)(A) provides that a rebuttable presumption shall arise if a pesticide's ingredients, metabolites, or degradation products induce "oncogenic effects in experimental mammalian species or in man as a result of oral, inhalation or dermal exposure." Many chemicals can react with nitrites to form N-nitroso compounds (56). Whether N-nitroso compounds can be formed from benomyl or its metabolites must be considered because N-nitroso compounds as a class are recognized as animal carcinogens (57).

Although there is not evidence at present that N-nitroso compounds are formed from benomyl or its metabolites, benomyl and its major plant metabolite MBC each have two possible sites of nitrosation. Formation of N-nitroso compounds, which is especially likely in formulations of benomyl with nitrogen fertilizers, might also occur after the pesticide is applied if there are nitrites present. Such formation is therefore possible in soil, water, air, plants, and animals including man.

Two papers (58, 59) dealing with the possible formation of N-nitroso compounds and induction of lymphosarcomas were evaluated for the Working Group (60). Both papers reported that neither MBC nor sodium nitrite alone produced tumors; tumors did develop in Swiss mice given high amounts of sodium nitrite (0.05 to 0.5 percent in drinking water) and administered MBC by gavage.

The fact that lymphosarcomas form in Swiss mice treated with MBC and nitrite but not in mice treated with MBC alone suggests that MBC and nitrite interact to create a stress that results in tumor production. However, the data do not provide evidence for *in vivo* production of N-nitroso MBC (58), nor do they establish that a metabolite of benomyl is involved in the carcinogenesis.

Furthermore, offspring of mice treated with MBC and nitrite during gestation developed tumors, whereas offspring of animals treated with MBC alone did not (59).

The potential formation of N-nitroso compounds of benomyl and MBC is a matter of serious concern. The Working Group solicits further information on the formation of N-nitroso compounds from benomyl or its metabolites, the conditions necessary for formation of such compounds, and their potential as carcinogenic agents.

LIST OF REFERENCES

1. Martin, H., Ed. 1972. *Pesticide Manual*, Ed. 3. British Crop Protection Council. Clacks Farm, Bailey, Ombersley, Droitwich, Worcester, England. p. 31.

2. *Evaluations of Some Pesticide Residues in Food*. 1974. WHO Pesticide Residues Series, No. 3. World Health Organization. Geneva. pp. 33–53.

3. Baude, F. J., J. A. Gardiner, and J. C. Y. Han. 1973. Characterization of residues on plants following foliar spray applications of benomyl. J. Agr. Food Chem. 21(6): 1084–1090.

4. Gardiner, J. A., J. J. Kirkland, H. L. Klopping, and H. Sherman. 1974. Fate of benomyl in animals. J. Agr. Food Chem. 22(3): 419–427.

5. Baude, F. J., H. L. Pease, and R. F. Holt. 1974. Fate of benomyl on field soil and turf. J. Agr. Food Chem. 22(3): 413–418.

6. Rhodes, R. C. and J. D. Long. 1974. Runoff and mobility studies on benomyl in soils and turf. Bull. Environ. Contam. Toxicol. 12(4): 385–393.

7. Kutz, F. W., November 24, 1976. Request for monitoring data on benomyl. Memorandum to Alma Shea, Project Manager, OSPR. With attachments. 8 pp.

8. Douch, P. G. C. 1973. The metabolism of benomyl fungicide in mammals. Xenobiotica 3(6):367–380.

9. Hammerschlag, R. S. and H. D. Sisler. 1972. Differential action of benomyl and methyl-2-benzimidazolecarbamate (MBC) in *Saccharomyces pastorianus*. Pest. Biochem. Physiol. 2:123–131.

10. Hammerschlag, R. S. and H. D. Sisler. 1973. Benomyl and methyl-2-benzimidazolecarbamate (MBC): Biochemical, cytological and chemical aspects of toxicity to *Ustilago maydis* and *Saccharomyces cerevesiae*. Pest. Biochem. Physiol. 3:42–54.

11. Siegel, M. R. and A. J. Zabbia, Jr. 1972. Distribution and metabolic fate of the fungicide benomyl in dwarf pea. Phytopathology 62:630–634.

12. Lowen. Cited in *1974 Evaluations of Some Pesticide Residues in Food*. WHO Pesticide Residues Series, No. 3. World Health Organization. Geneva. p. 40.

13. Peterson, C. A. and L. V. Edgington. 1969. Quantitative estimation of the fungicide benomyl using a bioautograph technique. J. Agr. Food Chem. 17(4):898–899.

Kilgore, W. W. and E. R. White. 1970. Decomposition of the systemic fungicide 1991 (Benlate). Bull. Environ. Contam. Toxicol. 5 (1):67–69.

14. Saito, E. August 30, 1977. Production data for benomyl. Memorandum to the files. Confidential.

15. Leitzke, J. S. March 29, 1977. Evaluation of acute aquatic hazard from benomyl. Memorandum to Richard Troast, Project Manager, OSPR. 1 p.

16. McCann, J. 1973. Fish Toxicity Laboratory Report No. 355. Animal Biology Laboratory, EPA. Beltsville, Md.

17. Knott, B. S. and C. D. Johnston. August 5, 1968. Fungicide 1991 safety evaluation of bluegill sunfish. Woodard Research Corporation. Submitted to EPA by E. I. du Pont de Nemours and Company on October 30, 1969. EPA Accession No. 091561.

18. McCann, J. A. June 24, 1977. Request for information on Benlate fungicide. Memorandum to Esther Saito, Project Manager, OSPR. With attachments. 6 pp.

19. Finley, M. T. August 1, 1977. Letter to Esther Saito, Project Manager, OSPR. With attachments. 27 pp.

20. Canton, J. H. 1976. The toxicity of benomyl, thiophanatemethyl, and BCM to four freshwater organisms. Bull. Environ, Contam. Toxicol. 16(2):214–218.

21. Styles, J. A. and R. Garner. 1974. Benzimidazolecarbamate methyl ester-evaluation of its effects *in vivo* and *in vitro*. Mutat. Res. 26:177–187.

22. De Brabander, M., R. Van de Veire, F. Aerts, S. Geuens, and J. Hoebeke. 1976. A new culture model facilitating rapid quantitative testing of mitotic spindle inhibition in mammalian cells. J. Nat. Cancer Inst. 56(2):357–363.

23. Seiler, J. P. 1976. The mutagenicity of benzimidazole and benzimidazole derivatives. VI. Cytogenetic effects of benzimidazole derivatives in the bone marrow of the mouse and the Chinese hamster. Mutat. Res. 40:339–348.

24. Sherman, H., R. Culik, and R. A. Jackson. 1975. Reproduction, teratogenic, and mutagenic studies with benomyl. Toxicol. Appl. Pharmacol. 32:305–315.

25. Zutshi, U. and B. L. Kaul. 1975. Studies on the cytogenetic activity of some common fungicides in higher plants. Cytobios 12:61–67.

26. Boyle, W. S. 1973. Cytogenetic effects of Benlate fungicide on *Allium cepa* and *Secale cereale*. J. Hered. 64(1):49–50.

27. Dassenoy, B. and J. A. Meyer. 1973. Mutagenic effect of benomyl on *Fusarium oxysporum*. Mutat. Res. 21:119–120.

28. Richmond, D. V. and A. Phillips. 1975. The effect of benomyl and carbendazim on mitosis in hyphae of *Botrytis cinerea* Pers. ex Fr. and roots of *Allium cepa* L. Pest. Biochem. Physiol. 5:367–379.

29. Davidse, L. C. 1973. Antimitotic activity of methyl benzimidazol-2-yl carbamate (MBC) in *Aspergillus nidulans*. Pest. Biochem. Physiol. 3:317–325.

30. Seiler, J. P. 1972. The mutagenicity of benzimidazole and benzimidazole derivatives. I. Forward and reverse mutations in *Salmonella typhimurium* caused by benzimidazole and some of its derivatives. Mutat. Res. 15:273–276.

31. Kappas, A., M. H. L. Green, B. A. Bridges, A. M. Rogers, and W. J. Muriel 1976. Benomyl—a novel type of base analogue mutagen? Mutat. Res. 40:379–382.

32. Seiler, J. P. 1973. The mutagenicity of benzimidazole and benzimidazole derivatives. II. Incorporation of benzimidazole into the nucleic acids of *Escherichia coli*. Mutat. Res. 17:21–25.

Seiler, J. P. 1975. The molecular mechanisms of benzimidazole mutagenicity: *In vitro* studies on transcription and translation. Biochem. Genet. 13(9/10):635–641.

33. Ficsor, G. and S. Bordas. Mutagenicity tests of benomyl and benomyl-containing products *in vitro* and in rodent host mediated assays in *Salmonella typhimurium*. Department of Biology. Western Michigan University, Kalamazoo. Unpublished.

34. Kappas, A., S. G. Georgopoulos, and A. C. Hastie. 1974. On the genetic activity of benzimidazole and thiophanate fungicides on diploid *Aspergillus nidulans*. Mutat. Res. 26 (1):17–27.

35. Busey, W. A. 1968. Acute inhalation exposure-Rats. Fungicide 1991 final report. Hazleton Laboratories, Inc., October 18, 1968. Submitted to EPA by E. I. du Pont de Nemours and Company on September 12, 1969. EPA Accession No. 050427.

36. Littlefield, N.A. 1969. Four-hour acute inhalation exposure-Dogs. Fungicide 1991 final report. Hazleton Laboratories, Inc., July 14, 1969. Submitted to EPA by E. I. du Pont de Nemours and Company on September 12, 1969. EPA Accession No. 050427.

37. Hofman, H. T. and P. Kirsch. Cited in *1974 Evaluations of Some Pesticide Residues in Food*. WHO Pesticide Residues Series No. 3. World Health Organization. Geneva. pp. 181.

38. Freudenthal, R. I. and A. P. Leber. 1977. Report on the validation of studies on benomyl teratogenicity and embryotoxicity in experimental animals. Battelle Laboratories Columbus, Ohio. Unpublished.

39. Shterberg, A. I. and A. M. Torchinsky, 1972. On the interrelationship of general toxic, embryotic, and teratogenic action of chemicals extraneous for the organism and the possibilities for prognosticating their influence on the antenatal period of ontogenesis. Vestnik Akad. Nauk SSR 3(27): 39–46.

40. Torchinski, A. M. 1973. The role of diets with different protein content in the manifestation of the teratogenous and embryotoxic effect of some pesticides. Vapr. Pitan. 3:76–80.

41. Saito, E. 1977. Benomyl in FDA Market Basket Survey. Memorandum to the files. 1 p.

42. Lehman, A. J. 1962. The annual per capita consumption of selected items of food in the United States. Quart. Bull. Assoc. Food Drug Off. 26(3):149–151.

43. Saito, E. June 22, 1977. Margin of safety for benomyl. Memorandum to Orville E. Paynter, Chief, Toxicology Branch, RD. With attachments. 3 pp.

44. Paynter, O. E. June 23, 1977. Margin of Safety—benomyl (Re Saito memo June 22, 1977). Memorandum to Esther Saito, Project Manager, OSPR. 1 p.

45. Severn, D. J. and D. W. Rucker. July 19, 1977. Preliminary analysis of human exposure to cadmium from the use of cadmium turf fungicides. Criteria and Evaluation Division, Office of Pesticide Programs, EPA. Unpublished.

46. Saito, E. August 1, 1977. Calculations of dermal exposure to benomyl from the use of benomyl rose spray.

47. Sherman, H. and W. C. Krauss. 1966. Acute oral test. Haskell Laboratory Report No. *100–66*, July 15, 1966. Submitted to EPA by E. I. du Pont de Nemours and Company on September 16, 1969. EPA Accession No. 003079.

48. Sherman, H. 1965. Acute oral test. Haskell Laboratory Report No. *174–65*, December 15, 1965. Submitted to EPA by E. I. du Pont de Nemours and Company on September 16, 1969. EPA Accession No. 003079.

49. Sherman, H., J. R. Barnes, and E. F. Stula. 1969. Long-term feeding study in rats with 1-butyl-carbamoyl-2-benzimidazolecarbamic acid, methyl esther [Int-1991; Benlate®; benomyl]. Haskell Laboratory Report No. *232–69*. August 15, 1969. Submitted to EPA by E. I. du Pont de Nemours and Company on September 16, 1969. EPA Accession No. 003070.

Sherman, H., J. R. Barnes, and E. F. Stula. 1970. Long-term feeding study in dogs with 1 - butycarbamoyl - 2-benzimidaole-carbamic acid, methyl ester [Int.-1991; Benlate®, benomyl]. Haskell Laboratory Report No. *48–70*. March 17, 1970. Submitted to EPA by E. I. du Pont de Nemours and Company on February 6, 1970. EPA Accession No. 091728.

50. Hornberger, C. S. 1969. Acute dust inhalation-rats. Haskell Laboratory Report No. *95–69*. April 24, 1969. Submitted to EPA by E. I. du Pont de Nemours and Company. September 16, 1969. EPA Accession No. 003073.

51. Anonymous. 1969. "Benlate" benomyl Fungicide—Summary of inhalation toxicity studies September 12, 1969. Submitted to EPA by E. I. du Pont de Nemours and Company. September 14, 1969. EPA Accession No. 050427.

52. Stringer, A. and M. A. Wright. 1973. The effect of benomyl and some related

compounds on *Lumbricus terrestris* and other earthworms. Pest. Sci. 4:165–170.

53. Stringer, A. and C. H. Lyons. 1974. The effect of benomyl and thiophanate-methyl on earthworm populations in apple orchards. Pest. Sci. 5:189–195.

54. Tomlin, A. D. and F. L. Gore. 1974. Effects of six insecticides and a fungicide on the numbers and biomass of earthworms in pasture. Bull. Environ. Contam. Toxicol. 12(4): 487–492.

55. Black, W. M. and D. Neely. 1975. Effect of soil-injected benomyl on resident earthworm populations. Pest. Sci. 6:543–545.

56. Elespuru, R. K. and W. Lijinsky. 1973. The formation of carcinogenic nitroso compounds from nitrite and some types of agricultural chemicals. Food Cosmet. Toxicol. 11:807–817.

57. Wolff, I. A. and A. E. Wasserman. 1972. Nitrates, nitrites and nitrosamines. Science 177(4043):15–19.

58. Borzsonyi, M. and M. Czik. 1975. Induction of malignant lymphomas in Swiss mice by N-nitroso compounds formed *in vivo*. Int. J. Cancer 15:830–838.

59. Borzsonyi, M., A. Pinter, A. Surjan, and I. Farkas. 1976. Transplacental induction of lymphomas in Swiss mice by carbendazim and sodium nitrite. Int. J. Cancer 17:742–747.

60. Baron, R. L. April 18, 1977. Evaluation report to Esther Saito, Project Manager, OSPR. 2 pp.

Mittelman, A. April 19, 1977. N-Nitroso benomyl review. Memorandum to Richard Troast, Project Manager, OSPR. With attachments. 25 pp.

**** PRODUCT SEARCH LISTING **** PAGE

08/18/77 FEDERALLY REGISTERED PRODUCTS CONTAINING BENOMYL

REGISTRANT *NAME AND ADDRESS*

* 000004 BONIDE CHEMICAL CO. INC.
2 KURZ AVE.
YORKVILLE NY 13495

********** PRODUCT NAME **********

**00196* BONIDE BENOMYL 50% WP

**00201* BENOMYL LAWN FUNGICIDE GRANULES

**00215* BONIDE BENOMYL 50% W.P. LAWN & ELM TREE DISEASE CONTROL

REGISTRANT *NAME AND ADDRESS*

* 000100 WASATCH CHEMICAL DIVISION ENTRADA IND INC
P O BOX 6219
SALT LAKE CITY UT 84106

********** PRODUCT NAME **********

**00476* MORGRO BENOMYL SYSTEMIC FUNGICIDE

REGISTRANT *NAME AND ADDRESS*

* 000352 E.I. DUPONT DE NEMOURS COMPANY
LEGAL DEPT. D7045
WILMINGTON, DE 19898

********** PRODUCT NAME **********

**00354* DU PONT BENLATE FUNGICIDE WETTABLE POWDER

**00357* DU PONT TERSAN 1991 TURF FUNGICIDE

**00358* DU PONT BENOMYL 50%

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08/18/77 FEDERALLY REGISTERED PRODUCTS CONTAINING BENOMYL

**CERTIFIABLE REGISTRANT 000352

**00277* DUPONT BENOMYL TECHNICAL

REGISTRANT *NAME AND ADDRESS*

* 000538 SCOTT O M & SONS COMPANY
MARYSVILLE OH 43040

********** PRODUCT NAME **********

**00066* PROTURF FERTILIZER PLUS DSB FUNGICIDE

**00132* SCOTTS PROTURF DSB FUNGICIDE

REGISTRANT *NAME AND ADDRESS*

* 000572 ROCKLAND CHEMICAL CO. INC.
P.O. BOX 809
CALDWELL, NJ 07006

********** PRODUCT NAME **********

**00254* ROCKLAND BENOMYL FUNGICIDE WETTABLE POWDER

**00256* ROCKLAND BENOMYL TURF FUNGICIDE GRANULES

REGISTRANT *NAME AND ADDRESS*

* 000769 WOOLFOLK CHEMICAL WORKS INC
PO BOX 528
FT VALLEY GA 31030

********** PRODUCT NAME **********

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08/18/77 FEDERALLY REGISTERED PRODUCTS CONTAINING BENOMYL

**CERTIFIABLE REGISTRANT 000769

**00415* SECURITY ROSE & TURF FUNGICIDE

REGISTRANT *NAME AND ADDRESS*

* 000802 LILLY CHAS P COMPANY MILLER RC DIV
7737 N.E. KILLINGSWORTH
PORTLAND, OR 97218

********** PRODUCT NAME **********

**00490* MILLER'S SYSTEMIC FUNGICIDE BENOMYL

REGISTRANT *NAME AND ADDRESS*

* 000829 SOUTHERN AGRI INSECT INC
PO BOX 218
PALMETTO FL 33561

********** PRODUCT NAME **********

**00217* SA-50 GRADE BENOMYL FUNGICIDE

REGISTRANT *NAME AND ADDRESS*

* 000865 GREEN LIGHT COMPANY
P.O. BOX 17985
SAN ANTONIO, TX 78217

********** PRODUCT NAME **********

**00125* GREEN LIGHT SYSTEMIC FUNGICIDE

REGISTRANT	*NAME AND ADDRESS*
* 000504	PRATT E C DIV GABRIEL CHEM LTD 204 21ST AVE PATERSON NJ 07505

********** PRODUCT NAME **********

**00224* PRATT BENOMYL 50W SYSTEMIC FUNGICIDE

REGISTRANT	*NAME AND ADDRESS*
* 001155	SEACOAST LABORATORIES INC 257 HIGHWAY 18 E BRUNSWICK NJ 08816

********** PRODUCT NAME **********

**00163* THIN LIGHT GRANULAR BENOMYL TURF FUNGICIDE

**00184* THIN LIGHT BENOMYL FUNGICIDE

REGISTRANT	*NAME AND ADDRESS*
* 001386	UNIVERSAL COOPERATIVES INC PO BOX 536 ALLIANCE OH 44601

********** PRODUCT NAME **********

**U 571* UNICO SYSTEMIC ROSE & ORNAMENTAL FUNGICIDE SPRAY

REGISTRANT	*NAME AND ADDRESS*
* 002125	SCIENCE PRODUCTS COMPANY INC 5801 N TRIPP AVE CHICAGO, IL 60646

********** PRODUCT NAME **********

**00064* SCIENCE BENOMYL

REGISTRANT	*NAME AND ADDRESS*
* 002165	PATTERSON CHEMICAL COMPANY INC 1400 UNION AVE KANSAS CITY, MO 64101

********** PRODUCT NAME **********

**00223* GREEN-UP BENOMYL SYSTEMIC FUNGICIDE

REGISTRANT	*NAME AND ADDRESS*
* 002342	KERR-MCGEE CHEMICAL CORP MGR PRC & LABELING KERR-MCGEE CENTER OKLAHOMA CITY OK 73102

********** PRODUCT NAME **********

**00750* GRO-TONE BENOMYL SYSTEMIC FUNGICIDE

**** PRODUCT SEARCH LISTING **** PAGE 6

08/18/77 FEDERALLY REGISTERED PRODUCTS CONTAINING BENOMYL

REGISTRANT *NAME AND ADDRESS*

* 005481 ARVAC CHEMICAL CORP
4100 EAST WASHINGTON BLVD
LOS ANGELES, CA 90023

********** PRODUCT NAME **********

**00138* ALCO SYSTEMIC FUNGICIDE

REGISTRANT *NAME AND ADDRESS*

* 007401 VOLUNTARY PURCHASING GROUP INC
PO BOX 460
BONHAM TX 75418

********** PRODUCT NAME **********

**00225* FERTI LOME SYSTEMIC FUNGICIDE WITH BENOMYL

REGISTRANT *NAME AND ADDRESS*

* 008764 FMC CORP
CITRUS MACHINERY DIV
PO BOX 552
RIVERSIDE CA 92502

********** PRODUCT NAME **********

**00017* FMC FRESHGARD 113 FUNGICIDE

**00027* FMC FUNGICIDE CONC. 202C

**** PRODUCT SEARCH LISTING **** PAGE 1

08/18/77 APPLICANTS FOR REGISTRATION OF PRODUCTS CONTAINING BENOMYL

REGISTRANT *NAME AND ADDRESS*

* 000557 SWIFT AGRICULTURAL CHEMICAL
CORP.
111 WEST JACKSON BOULEVARD
CHICAGO, IL 60604

********** PRODUCT NAME **********

**09608* PAR EX FERTILIZER PLUS BENOMYL (0.205%)

**05609* PAR EX FERTILIZER PLUS BENOMYL (0.287%)

**09610* PAR EX FERTILIZER PLUS BENOMYL (0.221%)

**09611* PAR EX FERTILIZER PLUS BENOMYL (0.169%)

**05612* PAR EX FERTILIZER PLUS BENOMYL (0.179%)

**09613* PAR EX FERTILIZER PLUS BENOMYL (0.191%)

**05614* PAR EX FERTILIZER PLUS BENOMYL (0.717%)

**09615* PAR EX FERTILIZER PLUS BENOMYL (0.319%)

**05616* PAR EX FERTILIZER PLUS BENOMYL (0.358%)

**09617* PAR EX FERTILIZER PLUS BENOMYL (0.409%)

**05618* PAR EX FERTILIZER PLUS BENOMYL (0.478%)

**09619* PAR EX FERTILIZER PLUS BENOMYL (0.239%)

**09620* PAR EX FERTILIZER PLUS BENOMYL (0.261%)

**05621* PAR EX FERTILIZER PLUS BENOMYL (0.573%)

**09622* PAR EX FERTILIZER PLUS BENOMYL (0.957%)

08/18/77 APPLICANTS FOR REGISTRATION OF PRODUCTS CONTAINING BENOMYL

REGISTRANT	*NAME AND ADDRESS*
* 000505	COOKE LABORATORY PRODUCTS 4759 S DUFFEE AVE PICO RIVERA CA 90660

********** PRODUCT NAME **********

**04701* COOKE SYSTEMIC FUNGICIDE

REGISTRANT	*NAME AND ADDRESS*
* 001671	FARMCRAFT, INC 8900 S W COMMERCIAL TIGARD OR 97223

********** PRODUCT NAME **********

**08945* FARMCRAFT BENLATE 1.5 DUST

REGISTRANT	*NAME AND ADDRESS*
* 002525	WILBUR ELLIS C . P. O. BOX 1286 FRESNO, CA 93715

********** PRODUCT NAME **********

**06567* RED-TOP ORTHO 4 BENOMYL 1 DUST

**06641* RED-TOP BENOMYL 1 DUST

08/18/77 APPLICANTS FOR REGISTRATION OF PRODUCTS CONTAINING BENOMYL

REGISTRANT	*NAME AND ADDRESS*
* 004561	PENNWALT CORP AGCHEM DIV. PENNWALT TECHNOLOGICAL CENTER P.O. BOX C KING OF PRUSSIA, PA 19406

********** PRODUCT NAME **********

**04365* DECCO SALT 20

**04391* DECCO SALT NO. 20

**04393* DECCO SALT NO. 20

**04396* DECCO SALT NO. 20

**04397* DECCO SALT NO. 20

**04398* DECCO SALT NO. 20

**04399* DECCO SALT NO. 20

**04400* DECCO SALT NO. 20

**04401* DECCO SALT NO. 20

**04402* DECCO SALT NO. 20

REGISTRANT	*NAME AND ADDRESS*
* 007404	NULIFE FERTILIZERS DIV OF HYGRADE FOOD PRODUCTS CORP PO BOX 883 TACOMA WA 98401

********** PRODUCT NAME **********

**06536* NULIFE 10-1-4 WITH BENLATE

**** PRODUCT SEARCH LISTING **** PAGE 4

08/16/77 APPLICANTS FOR REGISTRATION OF PRODUCTS CONTAINING BENOMYL

REGISTRANT *NAME AND ADDRESS*

* 008517 AMERICAN MACHINERY CORP
PO BOX 3228
ORLANDO FL 32802

********** PRODUCT NAME **********

**03345* PACRITE BENOMYL CITRUS FUNGICIDE CONCENTRATE

**03346* PACRITE SEALBRITE-81 CITRUS COATING CONTAINING BENOMYL

**03348* PACRITE SEALBRITE-80 CITRUS COATING CONTAINING BENOMYL

REGISTRANT *NAME AND ADDRESS*

* 008764 FMC CORP
CITRUS MACHINERY DIV
PO BOX 552
RIVERSIDE CA 92502

********** PRODUCT NAME **********

**07230* FRESHGARD 700

**07255* STA-FRESH 331

**07452* FUNGICIDE CONC. 50%

**05640* FUNGICIDE CONC. 50%

REGISTRANT *NAME AND ADDRESS*

* 010965 CALIFORNIA DEPT OF AGRICULTURE
WEED & VERTEBRATE PEST CONTROL 1220 N ST
SACRAMENTO CA 95814

********** PRODUCT NAME **********

**CONTINUE REGISTRANT CLOSED

**05518* ANY APPROPRIATE PRODUCT

**09919* ANY APPROPRIATE PRODUCT

**05520* ANY APPROPRIATE PRODUCT

**05521* ANY APPROPRIATE PRODUCT

**09922* ANY APPROPRIATE PRODUCT

**05523* ANY APPROPRIATE PRODUCT

REGISTRANT *NAME AND ADDRESS*

* 011093 MASTER NURSERYMEN'S ASSN C/O LEO DUPUICH
3620 1/2 MT DIABLO BLVD
LAFAYETTE CA 94549

********** PRODUCT NAME **********

**07129* 49ER GOLD STRIKE BENOMYL

REGISTRANT *NAME AND ADDRESS*

* 014775 AGRICH CHEMICAL COMPANY
PO DRAWER D
PLANT CITY FL 33566

********** PRODUCT NAME **********

**10505* BENOMYL 10% DUST

**** PRODUCT SEARCH LISTING **** PAGE 6

08/16/77 APPLICANTS FOR REGISTRATION OF PRODUCTS CONTAINING BENOMYL

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REGISTRANT *NAME AND ADDRESS*

* 035222 SOUTHERN CHEMICALS, INC.
204 N. ELM AVE, BOX 1480
SANFORD, FL 32771

********** PRODUCT NAME **********

**07169* BENOMYL-CAPTAN-STREPTOMYCIN DUST

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REGISTRANT *NAME AND ADDRESS*

* 037643 UNIVERSITY OF HAWAII-CC-CP
EXTENSION SERV-ENTOMOLOGY BRANCH
HONOLULU, HI 96822

********** PRODUCT NAME **********

**08588* BENOMYL (WP)

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REGISTRANT *NAME AND ADDRESS*

* 038655 N.Y.S. COLLEGE OF AGRICULTURE
& LIFE SCIENCES CORNELL UNIV.
ITHACA, NY 14853

********** PRODUCT NAME **********

**10456* NYS-DEWEY-BENOMYL II

**10469* NYS-DEWEY-BENOMYL

[FR Doc.77-34223 Filed 12-5-77;8:45 am]